Is early onset androgenetic alopecia related to hyperuricemia? A case control study

Loknath Ghoshal, Rabindranath Biswas, Dibyajyoti Sarkar

Department of Dermatology, Malda Medical College, Malda, West Bengal, India

(Received July 2022 Revised: November 2022 Accepted: December 2022)

Corresponding author: Loknath Ghoshal. Email: loknathghoshal@gmail.com

ABSTRACT

Introduction and Aim: Early onset androgenetic alopecia (AGA) ensues before age of 35 years and develops stage 3 in Hamilton-Norwood classification. AGA is more noticeable in males. Early onset AGA has been linked to hyperuricemia (a metabolic disorder characterised by elevated levels of serum uric acid) but has been explored inadequately. Hyperuricemia (HU) corroborates with the presence of hypertension, obesity, type 2 diabetes mellitus, metabolic syndrome and chronic kidney disease (CKD). Given the above and lack of data in this context, a study in this regard was necessary. This study was intended to relate the prevalence of HU and level of serum uric acid (SUA) levels in patients of early onset AGA versus matched controls and determine correlation between the severity of alopecia and serum uric acid and between the SUA and age (secondary objectives).

Materials and Methods: Each patient was evaluated by taking history, clinical examination and laboratory investigation.

Results: The groups were not different from each other with respect to age (p=0.5). The SUA in the AGA patient group was greater than in the control group; however the difference was not statistically significant. (p=0.2). AGA patients were found to have higher number of hyperuricemics as compared to the control group (Chi square test P=0.03, Odds ratio=0.39). There was no correlation between the severity of alopecia or the age of the subject with SUA.

Conclusion: Our study found that men who have early onset AGA tend to have higher serum uric acid levels; also, hyperuricemics are commoner in patients who have early onset AGA than in controls.

Keywords: Hyperuricemia; alopecia; metabolic disorder.

INTRODUCTION

Androgenetic alopecia (AGA) is the commonest cause of progressive hair loss.1 It occurs in genetically predisposed individuals and follows defined patterns. This pattern of hair loss is more noticeable in males and is mediated by gradual conversion of terminal hair to miniaturized hair. Premature AGA may be defined as AGA that ensues before the age of 35 years and downgrades to stage 3 of Hamilton-Norwood classification (1).

Numerous studies have found early-onset AGA to be related with systemic disorders such as obesity (2), hypertension (3), cardiovascular diseases (2) and metabolic syndrome (4). In fact, ‘strikingly increased’ risk of hyperinsulinemia and insulin-resistance (IR)-associated illnesses such as obesity, systemic hypertension, and dyslipidaemia in males with early onset AGA was found in one study (2).

Early onset AGA has also been linked to hyperuricemia (a metabolic disorder characterised by elevated levels of serum uric acid) but has been explored inadequately (4-5).

Hyperuricemia (HU) is considered present if serum uric acid (the end product of purine metabolism) level exceeds 7 mg/dL (6). HU is stated as primary or secondary depending upon its occurrence in idiopathic form or as a consequence of another concomitant disease or drug intake. HU has been found to affect as high as 25.8% of patients with hypertension or diabetes mellitus in India (7).

The prevalence of hyperuricemia is corroborated with the presence of hypertension, obesity, presence of metabolic syndrome, type 2 diabetes mellitus, and concomitant chronic kidney disease (CKD) (8-9). These are in fact the same morbidities stated earlier to be associated with early onset AGA. Given the above and the lack of data in this context, a study in this regard was found necessary.

We aimed to compare the prevalence of HU and level of serum uric acid (SUA) levels in patients of early onset AGA versus matched controls (primary
objective) We also aimed to determine correlation (if any) between the severity of alopecia and SUA (secondary objective); and to determine correlation (if any) between the SUA and age (secondary objective).

MATERIALS AND METHODS

This was a hospital based case control study in which we compared SUA values of patients with early onset AGA cases versus controls. AGA was diagnosed (case definition) clinically based on the distinctive pattern of fronto-temporal retreat of the hair line and diminishing of hair in the frontal and/or vertex areas. We used the basic and specific classification (BASP) and classified patients into mild, moderate and severe (10). Mild variety comprises the basic type L, M0, M1, and C1, and specific types V1 and F1; moderate AGA comprises basic type M2 and C2, and specific type V2 and F2. On the other hand the severe variety includes basic type M3, C3, U1, U2, and U3, and specific types V3 and F3 (10).

Institutional ethics committee permission was obtained before proceeding with the study. Patient consent was obtained from all subjects (legal guardians when the subject was minor).

All consecutive patients with the condition attending the outdoor department of this hospital were assessed for inclusion. Similar healthy volunteers (patients attending the outdoors for unrelated reasons) were requested to act as controls and consent obtained. The cases and controls were selected on the basis of computer generated random numbers.

Inclusion criteria

The cases were male AGA patients with disease onset between 18 and 35 years of age. Controls included male students, residents and other patients of the hospital without AGA. Hyperuricemia was specified as a serum uric acid (SUA) level of more than 7 mg/dl.

Exclusion criteria

use of hypouricemic or uricosuric agents; history of renal disease/ intake of nephrotoxic drugs; cardiovascular and cerebrovascular diseases; smoking and alcohol abuse; thyroid dysfunction, diabetes, and previous gouty arthritis and patients with severe systemic diseases and cancer.

Sample size calculation

Based on a similar study (4) where the mean± standard deviation was 6.25 ± 1.27 and 5.97 ± 1.15 mg/dl respectively for the case and control group with p<0.001 we calculated the sample size of 104 each in the case and control groups to be necessary for power of 0.8 and α of 0.05.

Study technique

The degree of AGA was described using the basic and specific classification (10) as stated previously. After incorporation into the study each patient was evaluated with thorough history taking, clinical examination and laboratory investigation. The data of each patient was recorded into an individual pre-structured case sheet. The individual case sheets were compiled into Excel tables (Microsoft Office for Windows 2016) for statistical analysis.

Statistical analysis

Quantitative data were described in mean ± Standard deviation; categorical data were stated as frequency and percentage. Quantitative data were tested using t-test; categorical variables were verified with the Chi Square test. Correlation between uric acid level and age was assessed using Pearson’s rho while severity of alopecia (ordinal data) and serum uric acid (continuous data) was analysed with Kendall’s Tau. Tests were done two tailed and the p value of <0.05 was considered significant. The statistical software Medcalc for PC.v19 was used for analyses. Null hypothesis (H0) assumed that occurrence of early onset AGA and hyperuricemia are independent variables.

RESULTS

The current study was intended to compare the uric acid level in patients of early onset androgenetic alopecia (AGA) with controls and determine whether hyperuricemia was related to the presence of early onset AGA in such subjects. We compared 104 cases of AGA to the same number of controls; the results are as stated as follows. The age of the subjects ranged from 18-35 years. The groups were not different from each other with respect to age composition (p=0.5).

The mean UA level in the case group was higher (5.9±1.8 mg/dl) than that in the control group (5.6±1.5mg/dl). The difference did not reach statistical significance (p = 0.2; Table 1).
Considered cut off value of serum uric acid as >7 mg/dl, 22 patients were found to be hyperuricemic (21.1%) while of the controls, 10 cases (9.6%) were hyperuricemic. The difference was significant (Chi square test P=0.03, Odds ratio=0.39, Table 2).

Table 2: Hyperuricemic versus non-hyperuricemic subjects in AGA versus non-AGA groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>AGA</th>
<th>Non-AGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperuricemic</td>
<td>22</td>
<td>10</td>
</tr>
<tr>
<td>Non-hyperuricemic</td>
<td>92</td>
<td>94</td>
</tr>
<tr>
<td>Odds ratio=2.52</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AGA=androgenetic alopecia

Most of the cases (76 patients, 73%) had the mild variety, while 27 (26%) patients had moderate alopecia while 1 patient (1%) had severe alopecia. We tested the serum uric acid values for correlation with or the severity of alopecia, but found there was no significant correlation (Kendall’s Tau=-0.0167, P=0.7983). They tested the serum uric acid levels for correlation with age of the subjects (case and control), but found none (Pearson’s rho=0.0473, p=0.4974).

DISCUSSION

Early onset AGA has been found to be associated with hypertension, insulin resistance, dyslipidemia and obesity. A few studies have suggested early onset AGA to be associated also with hyperuricemia (HU). The present study case control study was aimed at determining if AGA is associated with HU and was performed at a tertiary care centre in eastern India. The results obtained thereby are compared and contrasted with similar past studies as below.

The current study found mean serum uric acid level in AGA patients to be higher than in controls. Though the difference of means was not significant (P=0.2), the finding was consistent with the observation of Ma et al., (4) thus confirming the tendency of early onset AGA patients to have higher levels of serum uric acid as compared to controls.

Hyperuricemia was more common in the patient group than in the control group. The difference of proportion was found to be significant (Chi square test p<0.05). This finding also corroborated with that of Ma et al (4) thus endorsing the increased tendency of early onset AGA patients to have hyperuricemia.

Most of our patients (three-quarters) had mild alopecia while a quarter had moderate alopecia. We analysed for correlation between the severity of alopecia and serum uric and level. There was no such correlation. Thus severity of alopecia cannot possibly be used to predict serum uric acid level in a patient of early onset AGA.

When we analysed the study population (case and controls) for correlation between age and serum uric acid level, we found no significant correlation. The result can be expected as such as all major studies in this respect found no direct correlation. In fact, a large Japanese study found that the SUA levels in males diminished slightly from age 20 up to the seventh decade of life (11). AGA, and especially early onset AGA has commonly been seen to be associated with other metabolic diseases such as insulin resistance (IR) and dyslipidaemia in Asian as well as in Western populations (2,12). As regards the association between metabolic syndrome and HU, it is well-known that obese individuals consume high amounts of meat, which contain enormous amounts of purine. This results in raised uric acid concentration (13), while IR facilitates uric acid reabsorption in the renal tubules. The role of raised serum uric acid levels in this process is doubtful but is supposed to precede IR (14). Nevertheless, these outcomes point to metabolic dysfunction being a close companion, or even cause of hyperuricemia (15). Vasoactive substances produced during IR may cause endothelial dysfunction, causing perifollicular vasoconstriction. The resulting microvascular insufficiency and hypoxia at the hair follicle could add to the miniaturization of the same, resulting in AGA (16).

It may thus be inferred that the role of raised serum uric acid in early onset AGA is indirect, whereas
metabolic syndrome plays the role of an imperative and direct intermediary.

Limitations

Uric acid clearance involving 24-hour urine examination needed for accurate classification was not done in our setting. Also, patients with mild disease were not followed up for future possibility of increasing disease severity.

CONCLUSION

Our study found that men suffering from early onset AGA tend to have higher serum uric acid levels; also, hyperuricemia is commoner in men with early onset AGA than in controls. Thus, uric acid estimation should be considered in all cases of early onset AGA.

However, severity of alopecia cannot be used as an indicator of serum uric acid level; nor does age have any correlation with serum uric acid level.

ACKNOWLEDGEMENT

We sincerely thank all subjects for participating in the study.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

REFERENCES